Claims

What is claimed is:

- 1. A method for treating substance abuse in a patient in need thereof comprising administering a therapeutically effective amount of a compound of formula IV or a
- 5 pharmaceutically acceptable salt thereof:

$$CH_3O$$
 CH_2
 CH_2
 CH_3O
 (IV)

or a stereoisomer thereof.

2. The method of claim 1, wherein the compound of formula IV is

or a stereoisomer thereof.

3. The method of claim 1, wherein the compound of formula IV is a compound of formula VI or a pharmaceutically acceptable salt thereof:

15 VI.

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4. The method of claim 1, wherein the compound of formula IV is a compound of formula VII or a pharmaceutically acceptable salt thereof:

5. The method of claim 1, wherein the compound of formula IV is administered in an amount of about 0.1 mg to about 100 mg.

VII.

- 6. The method of claim 5, wherein the compound of formula IV is administered in an amount of about 1 mg to about 100 mg.
- 7. The method of claim 6, wherein the compound of formula IV is administered in an amount of about 5 mg to about 10 mg.
 - 8. The method of claim 1, wherein the compound of formula IV is orally administered.
 - 9. The method of claim 1, wherein the compound of formula IV is orally administered in the form of a tablet.
- 15 10. The method of claim 1, wherein the compound of formula IV is topically administered.
 - 11. The method of claim 10, wherein the compound of formula IV is topically administered in the form of a transdermal patch.
 - 12. The method of claim 1, wherein the substance abuse is a dependence on a compound selected from one or more of an opioid, an anxiolytic drug, a hypnotic drug, cocaine, a psychedelic agent, marijuana, an amphetamine, a hallucinogen, a phencyclidine, and a benzodiazepine.
 - 13. The method of claim 1, wherein the substance abuse is a dependence on alcohol.

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14. A method for treating one or more withdrawal symptoms associated with cessation from the use of an addictive substance in a patient in need thereof comprising administering an effective amount of compound of formula IV or a pharmaceutically acceptable salt thereof:

$$CH_3O$$
 CH_2
 CH_2
 CH_2
 CH_2
 CH_2
 CH_2
 CH_2

or a stereoisomer thereof.

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15. A method for decreasing the rate of relapse in a patient who had been previously addicted to an addictive substance comprising administering an effective amount of compound of formula IV or a pharmaceutically acceptable salt thereof:

$$CH_3O$$
 CH_2
 CH_2
 CH_2
 CH_2
 CH_2
 CH_3O

or a stereoisomer thereof.

16. A method for helping a patient stop using an addictive substance comprising
administering an effective amount of compound of formula IV or a pharmaceutically acceptable
salt thereof:

$$CH_3O$$
 CH_2
 CH_2
 CH_2
 CH_2
 CH_2
 CH_2

or a stereoisomer thereof.

20 17. A method for treating substance abuse in a patient in need thereof comprising administering a therapeutically effective amount of a cholinesterase inhibitor.

18. The method of claim 17, wherein the cholinesterase inhibitor is a compound of Formula (I), a stereoisomer thereof and/or a pharmaceutically acceptable salt thereof:

$$J \longrightarrow B \longrightarrow T$$
 $(CH_2)_q$
 $Q \longrightarrow K$

5 wherein J is

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- (a) a substituted or unsubstituted group selected from the group consisting of (1) phenyl, (2) pyridyl, (3) pyrazyl, (4) quinolyl, (5) cyclohexyl, (6) quinoxalyl, and (7) furyl;
- (b) a monovalent or divalent group, in which the phenyl may have one or more substituents selected from (1) indanyl, (2) indanonyl, (3) indenyl, (4) indenonyl,
 (5) indanedionyl, (6) tetralonyl, (7) benzosuberonyl, (8) indanolyl, and (9) C₆H₅-CO-CH(CH₃)-;
 - (c) a monovalent group derived from a cyclic amide compound;
 - (d) a lower alkyl group; or
- 15 (e) a group of R²¹-CH=CH-, in which R²¹ is hydrogen or a lower alkoxycarbonyl group;

B is -(CHR²²)_r-, -CO-(CHR²²)_r-, -NR⁴-(CHR²²)_r-, -CO-NR⁵-(CHR²²)_r-, -CH=CH-(CHR²²)_r-, -OCOO-(CHR²²)_r-, -OOC-NH-(CHR²²)_r-, -NH-CO-(CHR²²)_r-, -CH₂-CO-NH-(CHR²²)_r-, -(CH₂)₂-NH-(CHR²²)_r-, -CH(OH)-(CHR²²)_r-, =(CH-CH=CH)_b-, =CH-(CH₂)_c-, =(CH-CH)_d=, -CO-CH=CH-CH₂-, -CO-CH₂-CH(OH)-CH₂-, -CH(CH₃)-CO-NH-CH₂-, -CH=CH=CO-NH-(CH₂)₂-, -NH-, -O-, -S-, a dialkylaminoalkyl-carbonyl or a lower alkoxycarbony;

wherein R⁴ is hydrogen, lower alkyl, acyl, lower alkylsulfonyl, phenyl, substituted phenyl, benzyl, or substituted benzyl; R⁵ is hydrogen, lower alkyl or phenyl; r is zero or an integer of about 1 to about 10; R²² is hydrogen or methyl so that one alkylene group may have no methyl branch or one or more methyl branches; b is an integer of about 1 to about 3; c is zero or an integer of about 1 to about 9; d is zero or an integer of about 1 to about 5;

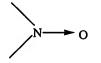
T is nitrogen or carbon;

Q is nitrogen, carbon or

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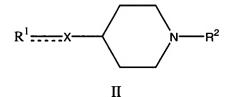


q is an integer of about 1 to about 3;

K is hydrogen, phenyl, substituted phenyl, arylalkyl in which the phenyl may have a substituent, cinnamyl, a lower alkyl, pyridylmethyl, cycloalkylalkyl, adamantanemethyl, furylmenthyl, cycloalkyl, lower alkoxycarbonyl or an acyl; and

is a single bond or a double bond.

19. The method of claim 17, wherein the cholinesterase inhibitor is a compound of Formula (II), a stereoisomer thereof and/or a pharmaceutically acceptable salt thereof:



wherein R¹ is a (1) substituted or unsubstituted phenyl group; (2) a substituted or unsubstituted pyridyl group; (3) a substituted or unsubstituted pyrazyl group; (4) a substituted or unsubstituted quinolyl group; (5) a substituted or unsubstituted indanyl group; (6) a substituted or unsubstituted cyclohexyl group; (7) a substituted or unsubstituted quinoxalyl group; (8) a substituted or unsubstituted furyl group; (9) a monovalent or divalent group derived from an indanone having a substituted or unsubstituted phenyl ring; (10) a monovalent group derived from a cyclic amide compound; (11) a lower alkyl group; or (12) a group of the formula R³-CH=C-, where R³ is a hydrogen atom or a lower alkoxycarbonyl group;

X is
$$-(CH_2)_{n^-}$$
, $-C(O)-(CH_2)_{n^-}$, $-N(R^4)-(CH_2)_{n^-}$, $-C(O)-N(R^5)-(CH_2)_{n^-}$,

 $-CH=CH-(CH_2)_n-$, $-O-C(O)-O-(CH_2)_n-$, $-O-C(O)-NH-(CH_2)_n-$, -CH=CH-CH=CO-,

 $-NH-C(O)-(CH_2)_{n^-}, -CH_2-C(O)-NH-(CH_2)_{n^-}, -(CH_2)_2-C(O)-NH-(CH_2)_{n^-},\\$

 $-CH(OH)-(CH_2)_n-, \ -C(O)-CH=CH-CH_2-, \ -C(O)-CH_2-CH(OH)-CH_2-, \\$

25 -CH(CH₃)-C(O)-NH-CH₂-, -CH=CH-C(O)-NH-(CH₂)₂-, a dialkylaminoalkylcarbonyl group, a lower alkoxycarbonyl group;

where n is an integer of 0 to 6; R⁴ is a hydrogen atom, a lower alkyl group, an acyl group, a lower alkylsulfonyl group, a substituted or unsubstituted phenyl group, or a substituted or unsubstituted benzyl group; and R⁵ is a hydrogen atom a lower alkyl group or a phenyl group;

R² is a substituted or unsubstituted phenyl group; a substituted or unsubstituted arylalkyl group; a cinnamyl group; a lower alkyl group; a pyridylmethyl group; a cycloalkylalkyl group; an adamantanemethyl group; or a furoylmethyl group; and

is a single bond or a double bond.

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20. The method of claim 17, wherein the cholinesterase inhibitor is a compound of Formula (III), a stereoisomer thereof and/or a pharmaceutically acceptable salt thereof:

$$(\operatorname{S})_{t} = (\operatorname{CHR}^{22})_{r} = (\operatorname{CH}_{2})_{q} \times (\operatorname{CH}_{2})_{q}$$

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wherein r is an integer of about 1 to about 10; each R²² is independently hydrogen or methyl; K is a phenalkyl or a phenalkyl having a substituent on the phenyl ring; each S is independently a hydrogen, a lower alkyl group having 1 to 6 carbon atoms or a lower alkoxy group having 1 to 6 carbon atoms; t is an integer of 1 to 4; q is an integer of about 1 to about 3; with the proviso that (S)_t can be a methylenedioxy group or an ethylenedioxy group joined to two adjacent carbon atoms of the phenyl ring.